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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/252,710	06/02/94	RIVIERE I	8141113

ANNE-LOUISE KERNER, PHD
HALE AND DORR, LLP AMERICAS
60 STATE STREET
BOSTON MA 02109-2711

HM22/0127

EXAMINER

FREDMAN, J

ART UNIT

1634

PAPER NUMBER

28

DATE MAILED: 01/27/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/252,710

Applicant(s)
Riviere et al

Examiner
Jeffrey Fredman

Group Art Unit
1634



☒ Responsive to communication(s) filed on Dec 7, 1998

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-4, 6-31, and 35-41 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) 38-41 is/are allowed.

☒ Claim(s) 1-4, 6-31, and 35-37 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1634

DETAILED ACTION

Transitional After Final Practice

1. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's second submission after final filed on December 7, 1998 has been entered.

Specification

2. The disclosure is objected to because of the following informalities:

The specification contains a table of contents which uses page numbers. Because the patent will be printed in columns different from the pagination in the table of contents, the table will be incorrect. Please delete the table of contents to comply with this objection.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. Claims 1-4 and 6-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP 608.04(a) states "Matter not in the original specification, claims, or drawings is usually new matter. Depending on circumstances such as the adequacy of the original disclosure, the addition of inherent characteristics such as chemical or physical properties, a new

Art Unit: 1634

structural formula or a new use may be new matter. See Ex parte Vander Wal, et al. , 1956 C.D. 11; 705 O.G. 5 (physical properties), Ex parte Fox , 1960 C.D. 28; 761 O.G. 906 (new formula) and Ex parte Ayers, et al. , 108 USPQ 444 (new use).”

Here, the new limitation to a “consensus splice site” as found in claims 1, 10 and 21, lacks basis in the original specification. The applicant cites the use of a splice site from the MOV-9 vector on page 29 of the specification in support of this broad term, but since many different consensus splice sites may exist, built around the basic GT-AG site, this term represents a broad term which is not supported by the narrower disclosure of the specification. In the absence of any specific support, this term represents new matter. Besides deletion of the term, which would moot the new matter rejection, two other possible courses of action may address this rejection. Amendment to limit the claims to the MOV-9 consensus splice site would appear acceptable, since this site is fully taught in the specification. Alternately, declarations or other evidence supporting a broader interpretation of the specification might be used to overcome this rejection.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

Art Unit: 1634

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 35-37 are rejected under 35 U.S.C. § 103 as being unpatentable over Temin in view of Bender et al. and Cone et al. Temin teaches the construction of various defective recombinant retroviral vectors based on murine leukemia viruses. These vectors can express a gene of interest, which may be virtually any gene because, as noted at page 163, there "are no reports of genes that cannot be expressed in retrovirus vectors." Helper cells transduced with these vectors are taught on page 156 of Temin. Temin further teaches that retroviral vectors may employ splice donor and acceptor sites (see page 162, constructs 5-7). Temin also teaches that stocks of helper-free virus may be prepared from vectors that do not have a selectable marker if the vectors are cotransfected into helper cells with a plasmid containing a selectable marker. Bender teaches that the packaging signal of vectors based on the Moloney murine leukemia virus extends into the gag region. Applicant claims vectors in which a splice donor and a splice acceptor are included, as well as an additional portion of the gag gene to enhance packaging. Cone et al. teach the construction of helper-free recombinant retroviral vectors and note on page 6353 that:

Art Unit: 1634

"...one can readily isolate lines such as Ψ -AM2275 that produce $>10^5$ recombinant virus per ml. These titers are high enough to facilitate the nonselective introduction of genes into 100% of a population of cells at high enough cell numbers to allow rapid analysis of DNA, RNA, or protein."

The claims are drawn to vectors that have splice donor and acceptor sites located between a 5' LTR and a 3' LTR and do not contain complete *gag*, *pol* or *env* genes or a complete selectable marker. One of ordinary skill in the art would have known from the combined teachings to make recombinant retroviral vectors that lack a complete selectable marker since the selectable marker gene would be unnecessary in view of the teaching of Cone et al. Cone provides specific motivation to perform transduction without a selectable marker stating "These titers are high enough to facilitate the nonselective introduction of genes into 100% of a population of cells at high enough cell numbers to allow rapid analysis of DNA, RNA, or protein (page 6353, column 1, paragraph 2)". This statement represents express motivation to perform nonselective transduction in order to permit rapid analysis of DNA, RNA or protein without necessitating the use of chemicals which might alter the experimental system. Further, Bender states "We conclude that the retrovirus packaging signal extends into the gag region. We have found that retroviral vectors containing the complete packaging signal allow more efficient gene transfer into a variety of cell types (page 1639, abstract)". The combined teachings of the prior art of Temin, Cone and Bender would have suggested such modifications to known vectors in the art as a means of regulating gene expression and increasing the efficiency of vector packaging. Therefore, the invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Art Unit: 1634

Allowable Subject Matter

6. Claims 38-41 are allowed.

7. The following is a statement of reasons for the indication of allowable subject matter:

These claims are drawn to specific retroviral vectors which inherently include the consensus splice site of claim 1 and which are expressly supported by the arguments described in the Cohen declaration (November 10, 1998) as discussed below.

Response to Declaration

8. The declaration under 37 CFR 1.132 filed December 7, 1998 is sufficient to overcome the rejection of claims 38-41 based upon 35 U.S.C. 103.

9. The Cohen declaration (November 10, 1998) evidences the fact that the prior art Jaffee reference required a 100 fold excess in order to transfect without selection, while the cited Cone reference utilizes only a 2 fold virus excess. The Cohen declarations both argue that a skilled artisan would not reasonably expect success with only a 2 fold virion excess in non-selective transfection. This argument is found persuasive with regard to the specific vectors for which it has been demonstrated, in the specification, the transfection functions as detailed in the specification (see figure 13 for example). Thus, the essential evidence is for unexpected results with regard to the claimed specific vectors.

Response to Arguments

10. Applicant's arguments filed December 7, 1998 have been fully considered and they are persuasive with regard to most of the amended current claims. Thus, as presently proposed,

Application/Control Number: 08/252,710

Page 7

Art Unit: 1634

claims 1-4 and 6-31, which are amended, overcome the cited prior art. However, in view of the new matter concern, these rejections over prior art are essentially in abeyance and would be reinstated if the new matter is withdrawn. The arguments are not persuasive as regards claims 35-37 which do not include the claimed limitations and thus are not covered by the arguments.


Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeff Fredman, Ph.D. whose telephone number is (703) 308-6568.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 180 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Group 1800 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).


Jeffrey Fredman
Patent Examiner
Art Unit 1634

January 19, 1999